C-REACTIVE PROTEINS IN THE SERA OF PATIENTS WITH LEPROSY

SISTER HILARY ROSS, B.S., CHARLES F. BUTLER AND RONALD B. LAUKAITIS, M.D.[1]
U. S. Public Health Service Hospital
Carville, Louisiana

It is apparent that the presence of C-reactive protein in human serum may have very broad clinical significance. Early investigators of this abnormal protein stressed its importance as an indicator of active rheumatic fever, but further work has demonstrated its presence in the sera of patients with a variety of other pathologic states. These include the collagen diseases, acute bacterial infections, myocardial infarction, and malignant neoplasms ([1, 3, 4]). It would seem, then, that this protein is a nonspecific indicator of an inflammatory reaction, whether it be bacterial or nonbacterial in origin. C-reactive protein is never found in normal human serum.

In 1955, Rabson ([2]) reported results of a study of C-reactive protein in the sera of 100 patients with leprosy. These were single determinations. In his concluding remarks mention was made of future studies involving serial determinations of this protein in leprosy. The present paper is a report of results obtained in studying serial C-reactive protein values in a number of leprosy cases.

MATERIALS AND METHODS

Over a period of two years, C-reactive protein (CRP) determinations were performed on the sera of 380 patients, of which 335 were of the lepromatous and 45 of the tuberculoid types. A total of 2,140 tests were performed on single specimens from 68 patients and multiple specimens from 312 patients. The numbers of determinations for each patient ranged between 1 and 73. The presence of the abnormal protein was determined with a commercial antiserum.[2] The capillary precipitin method recommended by the manufacturer was used: 1.5 cm. each of CRP antiserum and the patient's serum were drawn up into a capillary tube (external diameter 1 mm.) and incubated for 2 hours at 37°C. The degree of precipitation (0 to 4+) was read after overnight refrigeration at 4°C. It was felt that there was little to be gained from making any attempt at quantitative evaluation, so, for the purpose of the study, the tests were reported as either positive or negative.

RESULTS

TUBERCULOID LEPROSY

The results obtained in the 45 tuberculoid cases are shown in the first section of Table 1. Variable numbers of tests per patient were

[1] Biochemist, Medical Technician, and formerly Senior Assistant Surgeon, respectively.
[2] Schieffelin & Co., New York.

performed, ranging from 1 to 10. These were done at intervals of approximately two months spaced over the two-year period of the study.

TABLE 1.—*Results of repeated tests for C-reactive protein in (a) 45 tuberculoid cases, (b) 55 bacteriologically negative lepromatous cases, and (c) 280 bacteriologically positive lepromatous cases.*

No. of tests	No. of cases	CP[a]	IP[a]	CN[a]
		(a) Tuberculoid cases (45)		
1	9	4	—	5
2	13	2	4	7
3	15	2	7	6
4	2	0	2	0
5	2	0	1	1
5	4	1	3	0
	—	—	—	—
	45	9	17	19
		20%	37.8%	42.2%
		(b) Lepromatous cases, bacteriologically negative (55)		
1	11	6	—	5
2	13	1	3	9
3	13	2	2	9
4	9	0	6	3
5	3	0	2	1
6	2	0	1	1
7	—	—	—	—
8	—	—	—	—
9	—	—	—	—
10	1	—	1	—
11	1	—	1	—
12	2	1	1	—
	—	—	—	—
	55	10	17	28
		18.1%	30.9%	50.9%

(*c*) *Lepromatous cases, bacteriologically positive* (280)

1	48	13	—	35
2	58	11	24	23
3	52	10	18	24
4	23	4	13	6
5	13	1	6	6
6	2	1	1	0
7	4	0	4	0
8	2	0	2	0
9	5	3	2	0
10	6	1	5	0
11	7	1	6	0
12	12	2	9	1
13	7	3	3	1
14	13	3	10	0
15	9	2	7	0
16	6	1	5	0
17	1	0	1	0
18	2	0	2	0
19	—	—	—	—
20	1	1	0	0
20	9	6	3	0
	280	63	121	96
		22.5%	43.2%	34.2%

[a] CP = consistently positive; IP, inconsistently positive; CN, consistently negative.

Of the 9 tuberculoid cases with consistently positive results, it was possible to account for the positivity in 7 on the basis of such conditions as osteomyelitis, plantar ulcerations with infection, pulmonary tuberculosis, and postoperative status. It must be realized, however, that our figures represent only a small group of cases and can only be interpreted as indicating a trend rather than a definite conclusion.

LEPROMATOUS LEPROSY

Of the total of 335 lepromatous cases, 280 were "bacteriologically positive" at the time of the study, while 55 were "bacteriologically negative" and were classified as "apparently arrested."

Bacteriologically negative cases.—In the bacteriologically negative series, variable numbers of determinations were made, ranging from 1 to 12, with the majority being in the 2-4 group, as is to be seen in Table 1b.

Bacteriologically positive cases.—The "bacteriologically active" cases totaled 280. Variable numbers of determinations were done, ranging from 1 to 73, as shown in Table 1c.

In 96 of these bacteriologically positive cases the test for C-reactive protein was consistently negative. In 63 of these cases the test was positive. Later bacteriologic development of these cases was studied, as shown in Table 2.

TABLE 2.—*Bacteriologic activity of leprosy in relation to C-reactive protein after a lapse of two years.*

C-reactive protein test	Number of cases	Number of cases reverting to bacteriologic negativity
Consistently negative	96	29
Consistently positive	63	6

Table 2 shows the bacteriologic activity of lepromatous leprosy in relation to C-reactive protein after a lapse of two years. It appears that those patients who demonstrate negative C-reactive protein tests, as a group, bear a better prognosis in respect to assuming a "bacteriologically negative" status. Rabson (2) is of the opinion that failure to develop CRP in active lepromatous leprosy patients may represent some difference in host response. Whether this represents a factor of favorable or unfavorable prognostic significance can be determined only by long-term study of these cases. From our study of two years, failure to develop CRP in active lepromatous cases may have a favorable prognostic significance.

SUMMARY

The C-reactive protein test (CRP) performed by a capillary precipitation method was applied to the sera of 380 leprosy patients, among which 335 were of the lepromatous and 45 of the tuberculoid type.

A total of 2,140 tests were performed over a period of two years. The numbers of determinations for each patient ranged between 1 and 73.

Serial CRP tests in 45 tuberculoid cases showed 9 cases (20%) to be consistently positive, 17 cases (37.8%) inconsistently positive, and 19 cases (42.2%) consistently negative.

Of the 55 lepromatous cases that were bacteriologically negative ("arrested") at the end of the period, 28 (50.9%) were consistently negative, 17 (30.9%) were inconsistently positive, and 10 (18.1%) were consistently positive.

Of the 280 bacteriologically positive lepromatous cases, 96 (34.2%) were consistently negative, 121 (43.2%) inconsistently positive, and 63 (22.5%) consistently positive.

RESUMEN

La prueba de la proteína C-reactiva (PCR), ejecutada con una técnica de precipitación capilar, fué aplicada a los sueros de 380 leprosos, 335 de los cuales eran de la forma lepromatosa y 45 de la tuberculoidea.

Se verificó un total de 2,140 pruebas durante up período de dos años. El número de determinaciones para cada enfermo osciló entre 1 y 73.

Las pruebas PCR seriadas en los 45 casos tuberculoideos revelaron 9 casos (20%) constantemente positivos, 17 casos (37.8%) inconstantemente positivos y 19 casos (42.2%) constantemente negativos.

De los 55 casos lepromatosos que eran bacteriológicamente negativos ("estacionados") al terminar el período de prueba, 28 (50.9%) fueron constantemente negativos, 17 (30.9%) inconstantemente positivos y 10 (18.1%) constantemente positivos.

De los 280 casos lepromatosos que eran positivos bacteriológicamente, 96 (34.2%) resultaron constantemente negativos, 121 (43.2%) inconstantemente positivos y 63 (22.5%) constantemente positivos.

ADDENDUM: Since this manuscript was completed and submitted to the Public Health Service for permission for publication, a second previous report on the subject, by Ovid B. Bush, Jr., appeared in this JOURNAL **26** (1958) 123-126.

REFERENCES

1. KROOP, I. G. and SHACKMAN, N. H. Level of C-reactive protein as a measure of acute myocardial infarction. Proc. Soc. Exper. Biol. & Med. **86** (1954) 95-97.
2. RABSON, A. S. C-reactive protein in serum of patients with leprosy. Internat. J. Leprosy **23** (1955) 155-161.
3. SHETLAR, M. R., BULLOCK, J. A., SHETLAR, C. L. and PAYNE, R. W. Comparison of serum C-reactive protein, glycoprotein, and seromucoid in cancer, arthritis, tuberculosis and pregnancy. Proc. Soc. Exper. Biol. & Med. **88** (1955) 107-109.
4. STOLLERMAN, G. H., GLICK, S., PATEL, D. J., HIRCHFELD, I. and RUSOFF, J. H. Determination of C-reactive protein in serum as a guide to the treatment and management of rheumatic fever. American J. Med. **15** (1953) 645-655.